

EXHIBIT 6

Kentucky

Cabinet for Health and Family Services
Department for Public Health
Division of Epidemiology and Health Planning

Epidemiologic Notes & Reports



Volume 42 Number 2

March 2007

***Acinetobacter* Infections among Hospitalized Patients in Kentucky – 2006**

Emphasis on environmental cleaning and isolation precautions may prevent future outbreaks

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Background

Acinetobacter baumannii is a gram negative rod commonly found in the environment, including the soil, food, and water. Although *Acinetobacter* infections caused only about 7% of Intensive Care Unit (ICU) pneumonias in 2003, they are an increasingly common cause of nosocomial and ICU pneumonia (1). In September 2006, two Kentucky hospitals in different communities independently reported *Acinetobacter* outbreaks to the Kentucky Department for Public Health (DPH) within one week of each other. This report describes the outbreak investigation performed at these two facilities.

Investigation Methods

On September 29, 2006, DPH received notification of an *Acinetobacter* outbreak among patients in Hospital A. On October 3, the Centers for Disease Control and Prevention (CDC) notified DPH of a cluster of patients in a second facility (Hospital B), after being contacted directly by Hospital B infection control staff (CDC refers such state-based inquiries back to the State health department). An increase in case-patients from a baseline of approximately 1-2 per month to approximately 15 per month was reported for the months of August through October in Hospital A, and April through October in Hospital B. Patients were diagnosed with *Acinetobacter* based on wound, blood, sputum, urine, or bone culture obtained after a change

in the patient's clinical status occurred.

A total of 102 people were confirmed positive at the two facilities by clinical culture (30 in Hospital A and 72 in Hospital B). A CDC investigation was requested by DPH to provide additional personnel to assist with the large workload that would be generated by chart reviews, infection control compliance assessments, environmental evaluations, and lab testing inherent in a hospital investigation of this nature. Suzanne Beavers, MD, (the author of this article and Kentucky's Epidemic Intelligence Service (EIS) officer) began the investigation in early October, 2006 and subsequently led a team of four CDC investigators who arrived on October 30th. The primary goals of the investigation were to perform a case-control study to find risk factors associated with *Acinetobacter* infection, to examine infection control practices at the hospitals involved, and to look for ways to decrease transmission possibilities and incidence of infection at the two facilities.

A case was defined as a patient hospitalized during August 1-October 31, 2006 (Hospital A) or April 1-October 31, 2006 (Hospital B) who developed a positive culture for *Acinetobacter* on a clinical specimen. Patient charts were reviewed in order to evaluate potential risk factors such as admitting service, unit on admission, past medical history, surgeries during hospitalization, and need for ventilation or an invasive intravascular device. A control population was selected from patients without

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Acinetobacter who were hospitalized greater than or equal to the mean length of hospitalization for cases prior to obtaining the first positive culture. Isolation room practices were also observed in order to determine the level of compliance among hospital staff for contact and isolation precautions. In order to evaluate cleaning of high touch areas, a fluorescein compound visible with Wood's lamp was placed in patient rooms. The rooms were checked on subsequent days to determine if the fluorescein compound had been removed by daily cleaning, or cleaning of the room after patient discharge from the room. Environmental samples of high-touch areas in rooms containing patients positive for *Acinetobacter* were also taken.

Results

The mean age of cases was 43 years in Hospital A and 46 years in Hospital B. At Hospital A, 48% of cases were female; 25% of cases were female in Hospital B. The majority of patients (51.7% in Hospital A, 62.5% in Hospital B) cultured positive from a respiratory specimen. During the initial analysis, admission to a surgery service was associated with *Acinetobacter* infection, as was ICU admission. Artificial ventilation was also associated with a positive culture. The majority of patients (81.5% at Hospital A, 70.8% at Hospital B) had multi-drug resistant (MDR) *Acinetobacter* on culture (Figure 1).

Room observations revealed several instances in both facilities where isolation protocols were violated. Providers were occasionally observed entering the rooms without washing their hands. Providers occasionally entered the room without using barrier precautions such as gowns. Providers also were observed exiting the room without performing adequate hand washing.

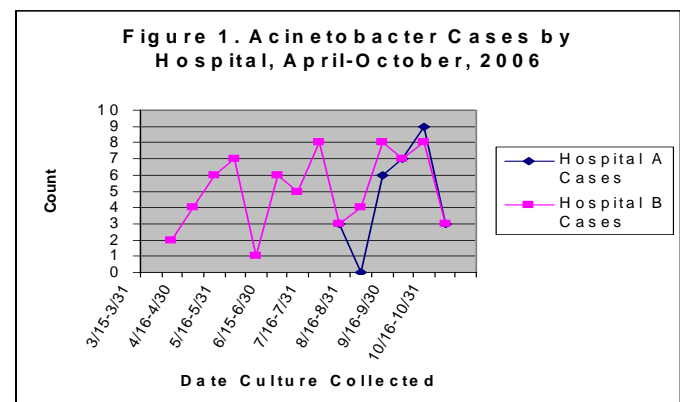
Evaluation of the environmental cleaning focused on several high-touch areas in the room. Fluorescein staining was consistently found in high-touch areas in the room after daily cleaning. Fluorescein could also be seen in high-touch areas following cleanings performed after a patient was discharged from the room.

Swabs performed by the hospitals prior to the in-

vestigative team's arrival did not reveal a point source of infection or one focus of environmental contamination. However, quantitative environmental testing at the two facilities is ongoing.

Hospital A closed its surgery ICU on the day of the team's arrival for thorough cleaning and decontamination and subsequently closed a second ICU for additional cleaning. In addition, enhanced isolation and decontamination procedures were also instituted throughout the hospital. Hospital A has subsequently reported lower incidence rates since October. Hospital B increased emphasis on following isolation precautions and has used fluorescein to evaluate and increase the importance of cleaning high-touch area, noting a decrease in cases as of February, 2007.

Figure 1. *Acinetobacter* cases by hospital, April-October 2006



Discussion

Acinetobacter baumannii is an increasing source of nosocomial infection nationwide. *Acinetobacter* species may cause pneumonia, wound infections, urinary tract infections, or bloodstream infections. Risk factors for *Acinetobacter* infection include recent surgery, admission to an ICU, need for antibiotics during hospitalization, and admission to a ward where other infected patients reside.

Results of the present investigation indicate the need for environmental cleaning staff education on the importance of cleaning high-touch areas. Areas such as bed rails, monitors, and door knobs are likely to be touched by patients and caregivers, and could be a source of spread of the implicated bacte-

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ria.

Acinetobacter species demonstrate the ability to survive for long periods in the environment. Previous researchers were able to culture *Acinetobacter* from a bedrail nine days after an infected patient was discharged from the room. Therefore, environmental contamination is often an important source of transmission of the organism. Previous outbreaks have found items such as common-use respiratory medications, ventilators, Bair Hugger temperature management units, mattresses, cellular phones, and curtains to be reservoirs of infection. Emphasis on environmental cleaning and observation of isolation precautions are consequently of particular importance in control of *Acinetobacter* outbreaks.

Another factor that has been of importance in the emergence of *Acinetobacter* nosocomial infections is the intrinsic antibacterial resistance of *Acinetobacter* and its ability to quickly acquire new resistance mechanisms. In fact, strains of *Acinetobacter* resistant to all antimicrobials have been isolated. *Acinetobacter* species are readily able to incorporate new genetic material into their DNA. This ability leads to the rapid acquisition of bacterial resistance, even from other types of bacteria such as *Pseudomonas*. The need for frequent use of antimicrobials in intensive care settings is also associated with the rapid acquisition of resistance.

Several methods have been used to control previous outbreaks. When a common source such as a ventilator is identified, cleaning the source properly or preventing patient exposure to the source has been effective in stopping the outbreak. Frequently, however, a common source is not identified. In these cases, increased emphases on environmental cleaning, use of active surveillance, and cohorting patients have been effective in halting outbreaks. Unit closure and environmental decontamination have also been beneficial.

Closing Notes

The outbreak investigations at the two facilities demonstrated the need for reinforcement of isolation precautions and enhanced environmental cleaning. Further analysis of data will continue in order to identify other risk factors and control

methods to assist in preventing future outbreaks. Additional work will continue with the hospitals to make recommendations for environmental cleaning as required.

References

1. Falagas ME, Kopterides P. Risk factors for the isolation of multi-drug *Acinetobacter baumannii* and *Pseudomonas aeruginosa*: a systematic review of the literature. *J of Hospital Infection* 2006;64:7-15.

World Tuberculosis Day – March 24

Despite diligent intervention efforts, TB disease remains a global threat

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Condensed from CDC National Center for HIV, STD, and TB Prevention, Division of TB Elimination

Each year, World Tuberculosis (TB) Day is recognized on March 24th. This annual event commemorates the date Robert Koch announced his discovery of the bacillus that causes TB. Around the world, TB programs, non-governmental organizations, and others take advantage of the increased interest and awareness that World TB Day generates concerning the international health threat that the disease presents. It is a day to recognize the collaborative efforts of all countries involved in fighting TB. TB can be cured, controlled, and with diligent efforts and sufficient resources, eventually eliminated.

In 1993, 404 active TB cases were reported in Kentucky, with a case rate of 10.7 cases per 100,000 population. Since 1993, TB case rates have been declining, suggesting that the nation is recovering from a resurgence of TB that occurred in the mid-1980s, and is back on track toward TB elimination. While the decrease in TB case rates is encouraging, the facts about TB continue to be alarming:

- TB continues to kill more people in the world each year than any other infectious disease.
- TB cases continue to be reported in every state.
- Multiple Drug-Resistant TB (MDR-TB) cases

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continue to be reported in almost every state.

- Extreme Drug-Resistant TB (XDR-TB) has emerged.
- An estimated 10 to 15 million persons in the U.S. are infected with *Mycobacterium tuberculosis*.
- Without intervention, approximately 10% of the 10 to 15 million persons infected in the U.S. will develop TB disease at some point in life.
- Certain other medical conditions increase the risk that a person with TB infection will develop TB disease (e.g. HIV, diabetes mellitus, cancers of the head and neck, jejunoileal bypass, solid organ transplantation, and other immunocompromising conditions).
- HIV infection is the strongest risk factor for progression from TB infection to TB disease. Approximately 50% of HIV-infected persons who become TB infected will develop disease within the first two years of exposure.

Where Are We Now?

TB remains a health threat to people around the world. Among infectious diseases, TB remains the second leading killer of adults in the world, with more than 2 million TB-related deaths each year. In addition to MDR-TB, the emergence of XDR-TB creates a greater and more deadly challenge of this disease. Whereas MDR-TB is drug resistant TB to two or more first line TB drugs, XDR-TB is defined by the World Health Organization (WHO) as TB that is resistant to the two main first line TB drugs, isoniazid (INH) and rifampin (RIF), as well as three of the six main classes of second line drugs. Poor treatment outcomes (patient not responding effectively to treatment) or failed treatment (patient not completing treatment or was lost to follow-up) are the largest contributing factors to the development of MDR-TB and XDR-TB. However, drug resistant strains are transmitted from person-to-person. Until TB is controlled, World TB Day will not be a celebration, but a valuable opportunity to educate the public about the devastation that TB can spread, and how it can be stopped.

TB in Kentucky

Reported cases of TB in Kentucky have reached a historic low. In 2006 there were 84 TB cases reported for a statewide rate of approximately 2.0

cases per 100,000 population. This rate places Kentucky well below the national TB case rate of 5.1 cases per 100,000 population, and below the state objective set in 1999 of reducing the verified TB case rate to 3.5 per 100,000 population. In 2005, the Kentucky TB Control Program reported 124 cases compared to 127 cases in 2004, 138 cases in 2003, and 146 cases in 2002. This case reduction illustrates the hard work and dedication of TB Control staff at the local health departments.

The future of TB Control in Kentucky

The lowering of case numbers is not, however, an indication that the war on TB has been won. Diligent efforts to identify and treat persons with TB infection that are at high risk for developing TB disease is the key to the continued reduction of incidences of TB disease in Kentucky. In addition, ensuring successful treatment outcomes to those with active disease is the main method for preventing MDR-TB and XDR-TB. To date in 2007, there have already been more than 20 active TB cases reported, a high case number for this early point in the year. To prevent resurgence, staff and resource levels must be maintained to allow Kentucky officials to have the tools required to continue working toward elimination of this most persistent disease.

Sexually-Transmitted Disease Update for Kentucky

Advancements in screening programs result in early detection

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Although sexually transmitted disease (STD) rates in Kentucky are not among the highest in the nation, they continue to be the most frequently reported of all communicable diseases statewide. *Chlamydia trachomatis* was the most frequently reported communicable disease in Kentucky in 2005, with 8,351 reports and an attack rate of 201.4 per 100,000 population. Gonorrhea was the second most frequently reported communicable disease in 2005 with 2,935 reports and a rate of 70.8 per 100,000 population. The same trend for these two diseases continued in 2006, as reported chlamydia

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cases increased 7.1% to 8,940 cases. Gonorrhea increased 11.1% with 3,277 reports.

Data released in November 2006 by the Centers for Disease Control and Prevention (CDC) revealed that Kentucky officially ranked 44th nationally in chlamydia and 31st in gonorrhea rates per 100,000 population in calendar year 2005. *Chlamydia trachomatis* is recognized as one of the most prevalent and potentially harmful STDs today. Men, women and infants are affected, but women bear a greater burden from infection, which is often asymptomatic. Infection in women can seriously compromise present and future reproductive health and may result in ectopic pregnancy, salpingitis, and pelvic inflammatory disease. Neonates of mothers infected with chlamydia and/or gonorrhea may develop an eye infection (ophthalmia neonatorum), and neonates of mothers infected with chlamydia could develop pneumonia within the first two months of birth. Many improvements in the laboratory identification of chlamydia and gonorrhea within the past decade have enabled aggressive screening programs to be initiated in each state to identify women with uncomplicated chlamydia and gonorrhea infection. Early detection can enable treatment before complications and debilitating sequelae associated with these infections occur. The target population for the screening programs has consisted of women of child bearing age seeking contraceptive, prenatal, STD, cancer screening, and other health services through public and private care facilities. The latest types of tests, known as nucleic acid probes, are more sensitive and specific, and enable the provider to screen patients for both chlamydia and gonorrhea from the same specimen collected by swab from the cervix or from a urine specimen. As a result of the newer testing procedures, there has been a significant decrease in the number of false negative results and an increase in the number of true positive results among persons screened.

Syphilis cases reported in calendar year 2006 totaled 188 compared to 129 cases in 2005. Included in this total were 73 patients with primary or secondary stage disease and 36 patients with early latent stage syphilis disease. The primary, secondary, and early latent stages of syphilis are collectively known as early syphilis because patients have been

infected for one year or less and, unless treated, potentially could spread infection to a sexual partner. The 109 patients reported with early syphilis in 2006 was a 34 case (45.3%) increase over 75 early syphilis cases reported in 2005. Included in the 109 early cases were 97 males and 12 females for a male to female ratio of 8:1. Syphilis case reporting is influenced by outbreaks that occur among populations at high risk for acquiring STDs. Over the past four years, a disproportionate number of early syphilis cases have been found in men who have sex with men. In calendar year 2006, 25 Kentucky counties reported one or more patients with early syphilis. Jefferson County reported the most cases with 52 reports, which included 49 males and 3 females. Fayette County had the second highest number of reports with 20 cases, all of whom were males.

Physicians and other healthcare professionals play a critical role in treating and preventing the spread of sexually transmitted diseases. CDC recently released a publication entitled *Sexually Transmitted Diseases Treatment Guidelines, 2006* to assist healthcare professionals in their efforts to diagnose and treat STDs. Requests for the 2006 treatment guidelines can be made through the Kentucky STD Program at (502) 564-4804. The guidelines are also available online at: <http://www.cdc.gov/std/treatment/2006/clinical.htm>.

Additionally, physicians and healthcare providers are urged to report STDs to their local county health department or to the STD Program at the Kentucky Department for Public Health. The Cabinet for Health and Family Services under 902 KAR 2:020 requires primary, secondary, early latent and congenital syphilis to be reported within 24 hours by fax at (502) 564-5715 or phone (502) 564-4804. Other STDs such as chlamydia, chancroid, gonorrhea, granuloma inguinale, lymphogranuloma venereum, late latent syphilis, and late manifest syphilis are to be reported within five business days. The Kentucky Reportable Disease Form (EPID 200-Rev. May/06) can be accessed online at: <http://chfs.ky.gov/providers/> or from the Kentucky STD Program at (502) 564-4804.

KENTUCKY EPIDEMIOLOGIC NOTES & REPORTS

Printed With State Funds
by the
Commonwealth of Kentucky
Cabinet for Health and Family Services
Department for Public Health
275 East Main Street
Frankfort, Kentucky 40621



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